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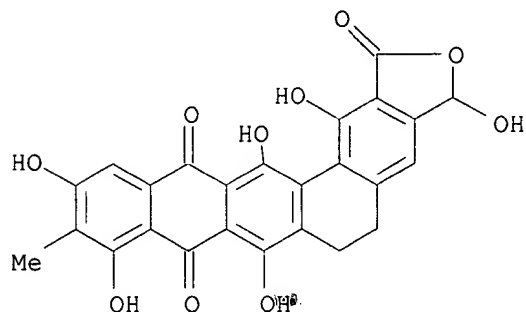
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Mondiale de la Propriété sous le numéro:

**WO 99/40908** (art.158 de la CBE).

L2 ANSWER 5 OF 473 REGISTRY COPYRIGHT 2001 ACS  
 RN 300578-79-4 REGISTRY  
 CN Naphtho[2',3':6,7]phenanthro[2,3-c]furan-1,8,13(3H)-trione,  
 5,6-dihydro-3,7,9,11,14,15-hexahydroxy-10-methyl- (9CI) (CA INDEX NAME)  
 OTHER NAMES:  
 CN **Desmethylnadurahydroxylactone**  
 MF C25 H16 O10  
 SR CA  
 LC STN Files: CA, CAPLUS



1 REFERENCES IN FILE CA (1967 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> s nadurahydroxylactone

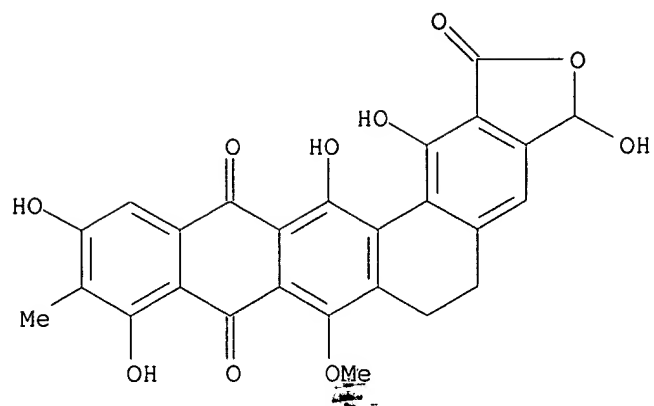
L3 2 MADURAHYDROXYLACTONE

=> s nadurahydroxylactone/cn

L4 1 MADURAHYDROXYLACTONE/CN

=> d

L4 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS  
 RN 160324-72-1 REGISTRY  
 CN Naphtho[2',3':6,7]phenanthro[2,3-c]furan-1,8,13(3H)-trione,  
 5,6-dihydro-3,9,11,14,15-pentahydroxy-7-methoxy-10-methyl- (9CI) (CA  
 INDEX NAME)  
 OTHER CA INDEX NAMES:  
 CN Naphtho[2',3':6,7]phenanthro[2,3-c]furan-1,8,13(3H)-trione,  
 5,6-dihydro-3,9,11,14,15-pentahydroxy-7-methoxy-10-methyl-, (.+-.)-  
 OTHER NAMES:  
 CN **Nadurahydroxylactone**  
 MF C26 H18 O10  
 CI COM  
 SR CA  
 LC STN Files: CA, CAPLUS, CASREACT, USPATFULL



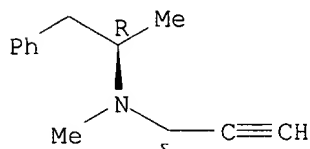
5 REFERENCES IN FILE CA (1967 TO DATE)  
5 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L5 ANSWER 8 OF 8 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.  
 TI **Antiviral** activity of norakin (triperiden) and related  
 anticholinergic antiparkinsonism drugs.  
 SO Acta Virologica, (1984) 28/6 (501-507).  
 CODEN: AVIRA2  
 AB In view of the coincidence of **antiviral** and antiparkinsonism  
 activities of amantadine, four antiparkinsonism drugs Norakin  
 (triperiden), Parkopan (trihexyphenidyl), Antiparkin  
 (diethylbenzhydramine) and Akineton (biperiden) were tested for  
**antiviral** activity in various virus-cell systems. Norakin  
 inhibited the replication of influenza A viruses in chick embryo  
 fibroblast, MDCK and Ehrlich. . . .  
 CT Medical Descriptors:  
 \*2 benzhydryloxy n,n diethylethylamine  
 \*drug efficacy  
 \*influenza virus  
 \*influenza virus a  
 \*measles virus  
 \*structure activity relation  
 cell culture  
 virus replication  
 priority journal  
 in vitro study  
 nonhuman  
 chicken  
 \*amantadine  
 \*antivirus agent  
 \*biperiden  
 \*rimantadine  
 \*trihexyphenidyl  
 \*triperidene  
**selegiline**  
 RN (amantadine) 665-66-7, 768-94-5; (biperiden) 1235-82-1, 514-65-8;  
 (rimantadine) 13392-28-4, 1501-84-4; (trihexyphenidyl) 144-11-6, 52-49-3;  
 (triperidene) 14617-17-5; (**selegiline**) 14611-51-9, 14611-52-0,  
 2079-54-1, 2323-36-6  
 AN 85025401 EMBASE  
 DN 1985025401  
 TI **Antiviral** activity of norakin (triperiden) and related  
 anticholinergic antiparkinsonism drugs.  
 AU Presber H.W.; Schroeder C.; Hegenscheid B.; et al.  
 CS Chain of Virology, Humboldt University, 1040 Berlin, Germany  
 SO Acta Virologica, (1984) 28/6 (501-507).  
 CODEN: AVIRA2  
 CY Czechoslovakia  
 DT Journal  
 FS 037 Drug Literature Index  
 047 Virology  
 030 Pharmacology  
 LA English

L2 ANSWER 12 OF 16 REGISTRY COPYRIGHT 2000 ACS  
 RN 14611-51-9 REGISTRY  
 CN Benzeneethanamine, N,.alpha.-dimethyl-N-2-propynyl-, (.alpha.R)- (9CI)  
 (CA INDEX NAME)  
 OTHER CA INDEX NAMES:  
 CN Benzeneethanamine, N,.alpha.-dimethyl-N-2-propynyl-, (R)-  
 CN Phenethylamine, N,.alpha.-dimethyl-N-2-propynyl-, L-(-)- (8CI)  
 OTHER NAMES:  
 CN (-)-Deprenil  
 CN (-)-Deprenyl  
 CN (-)-Selegiline  
 CN (R)-(-)-Deprenyl  
 CN Jumex  
 CN L-Deprenyl  
 CN l-Deprenyl  
 CN Selegiline  
 FS STEREOSEARCH  
 DR 172964-89-5  
 MF C13 H17 N  
 CI COM  
 LC STN Files: AGRICOLA, AIDSLINE, ANABSTR, BEILSTEIN\*, BIOBUSINESS,  
 BIOSIS,  
 BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CIN,  
 CSCHEM, DDFU, DIOGENES, DRUGNL, DRUGPAT, DRUGU, DRUGUPDATES, EMBASE,  
 IFICDB, IFIPAT, IFIUDB, IMSDIRECTORY, IPA, MEDLINE, MRCK\*, PHAR, PROMT,  
 SPECINFO, TOXLINE, TOXLIT, USAN, USPATFULL, VETU  
 (\*File contains numerically searchable property data)  
 Other Sources: WHO

Absolute stereochemistry. Rotation (-).

*desmethyl = w/o one methyl group*



742 REFERENCES IN FILE CA (1967 TO DATE)  
 9 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 743 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L1 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2001 ACS  
AN 1998:585951 CAPLUS  
DN 129:184245  
TI Application of aminergic agents in medications for treatment of viral  
infections of the central nervous system  
IN Ter Meulen, Volker; Riederer, Peter; Czub, Markus; Gerlach, Manfred  
PA Germany  
SO Ger. Offen., 6 pp.  
CODEN: GWXXBX  
DT Patent  
LA German  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 19708461	A1	19980827	DE 1997-19708461	19970218 <--

=> d ab

L1 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2001 ACS  
AB Viral (esp. retroviral) infections of the central nervous system are  
treated with an aminergic agent at a dose such as to establish a drug  
concn. in the target cells below that which affects viral gene  
expression.  
Suitable aminergic agents include dopaminergic agonists and antagonists,  
MAO-B inhibitors, D-methylselegiline, adamantine, and psychotropic and  
neuroleptic agents. Thus, in neonatal rats infected with murine leukemia  
virus (a microgliotropic retrovirus), development of spongiform  
encephalopathy was inhibited by i.p. injection of selegiline (0.05 mg/kg  
on days 15, 22, and 30 after infection).

=>

L11 ANSWER 6 OF 7 USPATFULL

SUMM . . . . fluconazole, ritonavir, itraconazole, miconazole, erythromycin and troleandomycin have been identified as inhibitors of the first-pass effect. These compounds, however, are **antiviral**, antimicrobial, or antifungal agents. Because of the heightened current awareness of the fact that overuse of such agents can result in resistant microbial strains, because some of the most effective inhibitors are antimicrobials, and because transplant and **HIV**-infected patients have compromised immune systems, the use of these inhibitors of the first-pass effect has significant drawbacks and, for example, . . . .

DETD . . . . or less, more preferably 50% or less. Examples include, in addition to those incorporated by reference above, ritonavir, saquinavir, indinavir, **L-deprenyl**, tacrolimus, cyclosporin A (Sandimmune.RTM.), cyclosporin A (Neoral.RTM.), nelfinavir, VX-478/141W94, felodipine, nifedipine and sumatriptan. Such co-formulations include the invention citrus-derived substance. . . .

AN 1999:151257 USPATFULL

TI Anti-first-pass effect compounds and citrus extract

IN Harris, James W., Cocoa Beach, FL, United States

PA Bioavailability Systems, L.L.C., Cocoa Beach, FL, United States (U.S. corporation)

PI US 5990154 19991123

AI US 1998-82939 19980522 (9)

PRAI US 1997-48183 19970530 (60)

DT Utility

EXNAM Primary Examiner: Ramsuer, Robert W.; Assistant Examiner: Solola, Taofiq

A

LREP Oblon, Spivak, McClelland, Maier & Neustadt, P.C.

CLMN Number of Claims: 2

ECL Exemplary Claim: 1

DRWN 4 Drawing Figure(s); 6 Drawing Page(s)

LN.CNT 894

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L11 ANSWER 7 OF 7 USPATFULL

DETD . . . . invention include analgesics, anesthetics, antifungals, antibiotics, antiinflammatories, anthelmintics, antidotes, antiemetics, antihistamines, antihypertensives, antimalarials, antimicrobials, antipsychotics, antipyretics, antiseptics, antiarthritics, antituberculosics, antitussives, **antivirals**, cardioactive drugs, cathartics, chemotherapeutic agents, corticoids (steroids), antidepressants, depressants, diagnostic aids, diuretics, enzymes, expectorants, hormones, hypnotics, minerals, nutritional supplements, parasympathomimetics, . . . .

DETD . . . . in the treatment of renal cell carcinoma, hairy cell leukemia, Kaposi's sarcoma, melanoma, and T-cell lymphoma, as well as an **antiviral** agent in the treatment of non-A,B-hepatitis, genital warts, Epstein-Barr virus, CMV, AIDS, and rhinovirus.

DETD . . . . red blood cells; the interleukins; interferon-gamma, a cytokine

protein produced by vertebrate cells following a virus infection and possessing potent **antiviral** effects; Vasotec.RTM., a antihypertensive (Enalapril maleate, Merck, Sharp & Dohme, West Point, Pa.) Capoten.RTM., a antihypertensive (Captopril, E. R. Squibb. . . .

DETD . . . . sequences of double-stranded DNA and are intended to inhibit selectively the transcription of disease-causing genes, such as viral genes, e.g., **HIV** and herpes simplex virus, and oncogenes, i.e., they stop protein production at the cell nucleus. These drugs

bind

directly to. . .

DETD . . . be utilized with a variety of pharmaceutical agents having tertiary amine groups. In a preferred embodiment, the pharmaceutical agent comprises **deprenyl**, as illustrated below: ##STR1##

DETD . . . apart from its carrier function. An example of a therapeutic chemical modifier is oligomeric or polymeric lysine (polylysine). Polylysine possesses **antiviral** and antibacterial activities, as well as a specific affinity for tumor cells in cancerous tissue. Ryser, H. J.-P. and Shen, . . .

DETD 5.3 Preparation of **deprenyl**-N-(morpholine-N-carboxyloxymethyl), iodide salt

DETD To a solution of **deprenyl** hydrochloride (146 mg, 0.654 mmol) in acetonitrile (10 ml) was added the iodo carbamate prepared above (180 mg, 0.654 mmol).. . .

DETD 6.19 Preparation of **deprenyl**-N-ethoxycarboxyloxymethyl, iodide salt

DETD To a solution of **deprenyl** (424 mg, 2.3 mmol) in acetonitrile (5 ml) was added chloromethyl ethyl carbonate (315 mg, 2.3 mmol) and sodium iodide. . .

DETD 6.20 Preparation of **deprenyl**-N-octyloxycarboxyloxymethyl, iodide salt

DETD To a solution of **deprenyl** (170 mg, 0.91 mmol) in acetonitrile (5 ml) was added iodomethyl octyl carbonate (290 mg, 0.91 mmol). The reaction mixture. . .

DETD 6.21 Preparation of **deprenyl**-N-butyroyloxymethyl, iodide salt

DETD To a solution of **deprenyl** (139 mg, 0.743 mmol) in acetonitrile (5 ml) was added iodomethyl butyrate (169 mg, 0.743 mmol). The reaction mixture was. . .

DETD 6.22 Preparation of **deprenyl**-N-pivaloyloxymethyl, iodide salt

DETD To a solution of **deprenyl** (240 mg, 1.28 mmol) in acetonitrile (5 ml) was added chloromethyl 2,2-dimethylpropionate (193 mg, 1.28 mmol) and sodium iodide (192. . .

DETD 6.23 Preparation of **deprenyl**-N-acetoxymethyl, bromide salt

DETD To a solution of **deprenyl** (100 mg, 0.654 mmol) in acetonitrile (5 ml) was added bromomethyl acetate (146 mg, 0.654 mmol). The reaction mixture was. . .

DETD To a solution of **deprenyl** (424 mg, 2.3 mmol) in acetonitrile (5 ml) was added chloromethyl ethyl carbonate (315 mg, 2.3 mmol), followed by sodium. . .

DETD . . . 1 hr

carboxamide), chloride salt

cisapride-N-(6-trimethylammoniohexanoyloxymethylammonio), diiodide salt

1 hr

cisapride-N-acetoxymethylammonio, iodide salt

6.5 min

cisapride-N-butyroyloxymethylammonio, iodide salt

7.6 min

cisapride-N-ethoxycarboxyloxymethylammonio, iodide salt

4.4 min

cisapride-N-lauroyloxymethylammonio, iodide salt

5.4 min

**deprenyl**-N-acetoxymethyl, bromide salt

4.2 min

**deprenyl**-N-benzoyloxymethyl, iodide salt

5 min

**deprenyl**-N-butyroyloxy-1-ethyl, bromide salt

28 min

**deprenyl**-N-butyroyloxymethyl, iodide salt

17 sec

**deprenyl**-N-ethoxycarboxyloxymethyl,



71 sec  
iodide salt  
deprenyl-N-octyloxycarbonyloxymethyl,  
26 sec  
iodide salt  
deprenyl-N-pivaloyloxymethyl, iodide salt  
20 min  
methotrexate-bis-(4-trimethylammoniobutyroyl-  
1.8 hr  
oxymethyl ester), diiodide salt  
morphine-6-O-(trimethylammoniobutyrate  
26 hr  
chloride, hydrochloride salt  
progesterone-3-(4-N,N,N-trimethylammonio-  
3 hr  
butyrate enol ester, bromide salt  
progesterone-3-betainoyl enol. . .  
AN 97:17918 USPATFULL  
TI Compositions and methods for enhanced drug delivery  
IN Hale, Ron L., Woodside, CA, United States  
Lu, Amy, Los Altos, CA, United States  
Solas, Dennis, San Francisco, CA, United States  
Selick, Harold E., Belmont, CA, United States  
Oldenburg, Kevin R., Fremont, CA, United States  
Zaffaroni, Alejandro C., Atherton, CA, United States  
PA Affymax Technologies N.V., Middlesex, England (non-U.S. corporation)  
PI US 5607691 19970304  
AI US 1995-449188 19950524 (8)  
RLI Continuation of Ser. No. US 1993-164293, filed on 9 Dec 1993, now  
abandoned which is a continuation-in-part of Ser. No. US 1993-77296,  
filed on 14 Jun 1993, now abandoned which is a continuation-in-part of  
Ser. No. US 1992-898219, filed on 12 Jun 1992, now abandoned And a  
continuation-in-part of Ser. No. US 1993-9463, filed on 27 Jan 1993,  
now  
abandoned  
DT Utility  
EXNAM Primary Examiner: Levy, Neil S.  
LREP Stevens, Lauren L.  
CLMN Number of Claims: 5  
ECL Exemplary Claim: 1  
DRWN No Drawings  
LN.CNT 5349  
CAS INDEXING IS AVAILABLE FOR THIS PATENT.